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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,086	10/24/2001	Avi J. Ashkenazi	GNE.2630P1C64	4093

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,086	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63,66,68-70 and 74-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63,66,68-70 and 74-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 63, 66, 68-70 and 74-84 are pending in the instant application. Claims 58-62, 64, 65, 67 and 71-73 have been canceled, claims 63, 66, 68, 69 and 74 have been amended and claims 78-84 have been added as requested by Applicant in the Amendment filed November 18, 2004.

Withdrawn Objections and Rejections

2. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 78-84 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, because the fragments recited, at least 20, 50, 60, 70, 80, 90 or 100 nucleotides in length, were not disclosed in the application.

Maintained Rejections

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 63, 66, 68-70 and 74-77 remain rejected and new claims 78-84 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for reasons of record in the previous office action, mailed May 19, 2004, at pages 4-7 and below.

Applicants' arguments (pages 14-19, Paper filed Nov. 18, 2004) have been fully considered but are not deemed persuasive.

Applicants traverse the rejection and discuss the legal standard for utility on pages 14-16, and starting on page 16 discuss the proper application of the legal standard. Applicants rely on the gene amplification data for patentable utility for the PRO274 nucleic acid, and explain the gene amplification assay of Example 114, in which PRO274 is amplified two fold to 3.053 fold in three types of human primary lung tumors, and which Applicants assert is significant and therefore the PRO274 gene has utility as a diagnostic marker of lung cancer. Applicants submit a Declaration signed by Dr. Thomas D. Wu, in which he describes 3 sets of microarray experiments in which lung tissue samples from 19 healthy patients and from at least 76 patients having a variety of different types of lung tumors were compared. Dr. Wu found that for each type of lung tumor mentioned at least 10% of the patients with that type of lung tumor have overexpressed levels of PRO270 mRNA in their tissue samples compared to normal lung tissue

samples from patients without lung cancer. Dr. Wu states that it is his opinion that when, the mRNA of a gene is overexpressed in at least about 10% of the lung tumors of the same type, the gene is biologically significant as a lung tumor marker, and it is well known in the art that a lung tumor marker that is expressed in each type of lung tumor is very rare.

The Wu Declaration filed under 37 CFR 1.132, filed Nov. 18, 2004 is insufficient to overcome the rejection of claims 63, 66, 68-70 and 74-84 as set forth in the last Office action because: while the declaration provides further support that the mRNA is overexpressed in about 10% of all lung cancers of various different types and *could* possibly be useful as a cancer marker, the declaration does not provide any information on the extent of overexpression of the PRO274 mRNA, or how significant the overexpression is. It should be noted that the statement on page 17 of the response, lines 12-14, is not accurate with respect to the Wu declaration. On page 17 of the response is written:

> "As stated in the Declaration, Dr. Wu found that for each type of the lung tumors listed above, the mRNA expression level of PR0274 was at least 10% or greater in the lung tumor tissues compared to normal lung tissues."

What the Wu declaration states is that the mRNA is overexpressed in about 10% of all lung cancers of various different types, which is different from that stated above. While the specification provides data that the PRO274 gene is overexpressed in three out of eighteen lung cancers (17%) at a level of two to about three fold over expression in normal lung tissue, the Wu declaration does not provide any information on the degree of overexpression in the cancer samples. For example, is the overexpression 1.5 fold, 2 fold or 5 fold over normal? Without this

information the accuracy and significance of the results of the microarrays cannot be adequately assessed.

Applicants also provide the Declaration by Dr. Audrey Goddard, in which she states that a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer. Applicants assert that as the TaqMan realtime PCR method has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification, one of ordinary skill in the art would find it credible that PRO274 is a diagnostic marker of human lung cancer.

The Goddard Declaration filed under 37 CFR 1.132, filed Nov. 18, 2004 is insufficient to overcome the rejection of claims 63, 66, 68-70 and 74-84 as set forth in the last Office action because: while the declaration and supporting references are convincing that the TaqMan realtime PCR method is very sensitive and can identify amplified genes, it is well known that aneuploidy is a common feature of most human cancers, and the data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid.

The requirement for further research requirements to determine if the nucleic acid is a diagnostic marker makes it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is

directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. For all of these reasons, the rejections are maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, cle, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5.1 Claims 63, 66, 68-70 and 74-77 also remain rejected and new claims 78-84 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5.2 New claims 78-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claims 78-84 encompass an isolated nucleic acid molecule at least 20, 50, 60, 70, 80, 90 or 100 nucleotides in length that specifically hybridizes under the stringent conditions recited to the nucleic acid sequence of SEQ ID NO: 6 or the full-length coding sequence of the cDNA deposited under ATCC accession number 209786. Applicants canceled claims 58-62 and 71-77, and therefore the rejection of those claims is moot. However, new claims 78-84 are now rejected.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The specification discloses only a single sequence, SEQ ID NO: 6, that meets the limitations of the claims. As previously stated, one cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQZII 1481 at 1483. In *Fiddes,* claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In this case, applicants have described a single sequence. This case is also analogous to that in *Amgen v. Chugai*, 18 USPQ 2d 1017 (1991), in which it was found that conception may not be achieved until reduction to practice in cases involving cloning genes. In this case, applicants have no conception of which of the thousands of possible nucleic acids would hybridize to the nucleic acid molecule of SEQ ID NO: 6.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. Chugai Pharmaceutical Co. L td.*, 18 USPQ2d 1016.

Therefore, the nucleic acid sequence of SEQ ID NO: 7, but not the full breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Rejections over Prior Art

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. New claims 78-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al., Science, Vol. 289, July 14, 2000, pages 265-270, for reasons of record in the previous Office Action, mailed May 20, 2004, at page 11, and below.

New claims 78-84 encompass an isolated nucleic acid molecule at least 20, 50, 60, 70, 80, 90 or 100 nucleotides in length that specifically hybridizes under the stringent conditions recited to the nucleic acid sequence of SEQ ID NO: 6 or the full-length coding sequence of the cDNA deposited under ATCC accession number 209786. Because there are only 4 mismatches between the nucleic acid of Ho et al. and nucleotides 1-2943 of SEQ ID NO: 6 of the instant invention, nucleic acid molecules of Ho et al. at least 20, 50, 60, 70, 80, 90 or 100 nucleotides in length would specifically hybridize to the nucleic acid molecule of SEQ ID NO: 6 of the instant invention under those hybridization conditions.

Applicants traverse the rejections and assert that they are entitled to the effective filing date of February 11, 2000, so that Ho et al. is not prior art. Applicants' arguments have been fully considered but are not deemed persuasive, because the gene amplification assay fails to provide a patentable utility for the nucleic acid, for reasons discussed above, and therefore the effective filing date is October 24, 2001, and the rejection is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

7. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (571) 272-0829.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER